

Two cases of myotonic dystrophy manifesting various ophthalmic findings with genetic evaluation

Min Ji Kang, Hye Bin Yim, Hyung Bin Hwang

We report two cases of myotonic dystrophy in one family; both diagnosed from genetic analysis following ophthalmic indications, but before the manifestation of systemic symptoms. A 39-year-old female visited our clinic for routine examination. Mild ptosis, sluggish pupillary response, and bilateral snowflake cataracts were found. Fundus examination revealed an increased cup-to-disc ratio (CDR) in both eyes and a defect in the retinal nerve fiber layer in the right eye. Intraocular pressure was low, but within the normal range in both eyes. Because cataracts are characteristic of myotonic dystrophy, we suggested that her 14-year-old daughter, who did not have any systemic complaints, undergo ophthalmic examination. She also had mild ptosis and snowflake cataracts. Both patients underwent genetic evaluation and were diagnosed with myotonic dystrophy caused by unstable expansion of cytosine-thymine-guanine trinucleotide repeats in the dystrophin myotonia-protein kinase gene. Ophthalmologists can diagnose myotonic dystrophy based on clinical and genetic findings, before the manifestation of systemic abnormalities.

Key words: Blepharoptosis, cataract, genes, myotonic dystrophy

Myotonic dystrophy, or dystrophin myotonia (DM), is the most common muscular dystrophy in adults, with a prevalence of approximately 1/8000.^[1] Myotonia and multisystemic involvement are two important characteristics.^[2] The inheritance pattern is autosomal dominant, and the mutation responsible for myotonic dystrophy is an expansion of a tandem repeat.^[3]

Ocular complications can be the first clinical sign, and the most common finding is a cataract. Nearly 100% of myotonic dystrophy patients have bilateral iridescent cataracts.^[4] Here, we report two cases of myotonic dystrophy in one family, both

of whom were suspected of myotonic dystrophy based only on ophthalmic manifestations.

Case Report

A 39-year-old female visited our clinic for ophthalmic routine examination. She had no underlying disease but complained of slight muscle and general weakness, and her brother had died of myotonic dystrophy several years earlier.

Her best-corrected visual acuity was 16/20 in both eyes, and intraocular pressure was 12 mmHg in the right eye and 13 mmHg in the left eye. She had mild bilateral ptosis with margin reflex distance 1 of 0.5 mm in both eyes, and levator function test of 9 mm in both eyes [Fig. 1]. Alternative covering tests found orthophoria in her primary gaze, while ocular motility was normal. Poor response to mydriatics was noted, and characteristic bilateral snowflake cataracts were observed on the slit lamp examination [Fig. 2]. Dilated fundus examination found an increased CDR of 0.5/0.5, vertical/horizontal in both eyes, and a defect in the inferotemporal retinal nerve fiber layer in her right eye [Fig. 3].

We noticed ptotic appearance in her 14-year-old daughter, who was also present and who did not have any systemic or ocular complaints, which suggested ophthalmic examination. The examination found the visual acuity of 20/20 in the right eye and 18/20 in the left eye, and intraocular pressure of 13 mmHg in the right eye and 16 mmHg in the left eye. Similar to her mother, mild bilateral ptosis with levator function of 9 mm in both eyes, poor response to mydriatics, and bilateral snowflake cataracts were noted [Fig. 4]. Ocular motility was unimpaired, and cover testing found orthophoria in the primary position. Fundus examination showed no abnormality.

Based on these ophthalmic findings, the patient and daughter were referred to the Department of Laboratory Medicine for genetic evaluation for myotonic dystrophy using the Southern blot polymerase chain reaction. Unstable repeats of 550 cytosine-thymine-guanine (CTG) units in the 3' untranslated region of the DM-protein kinase (DMPK) gene were found in both patients, indicating classic myotonic dystrophy Type 1 [Fig. 5]. Based on ophthalmic indications, both patients were diagnosed with myotonic dystrophy Type 1 on genetic examination before the manifestation of other systemic changes [Fig. 6].

Discussion

Myotonic dystrophy has heterogeneous clinical features including myotonia, progressive muscle weakness and atrophy,

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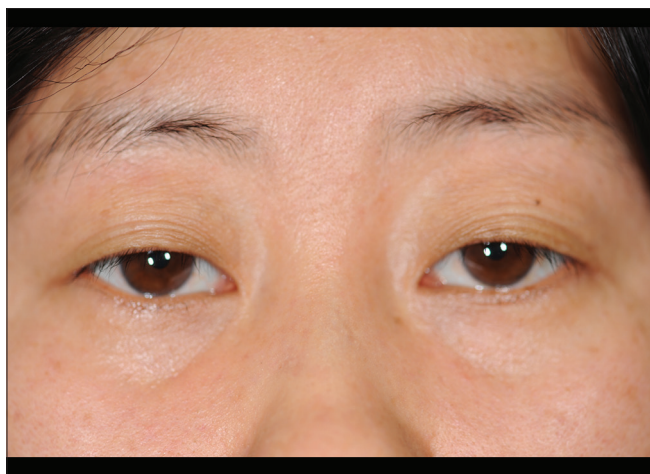


Figure 1: Bilateral ptosis in myotonic dystrophy

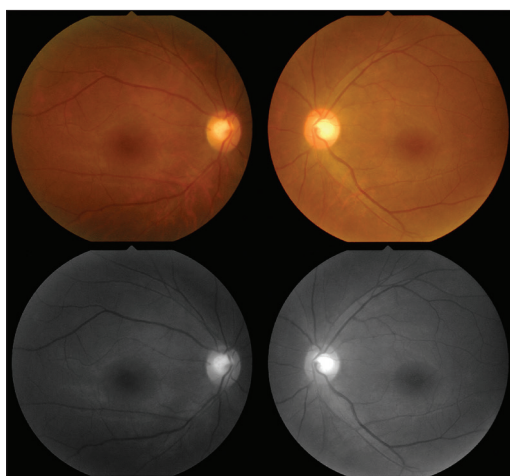


Figure 3: High cup-to-disc ratio with inferotemporal retinal nerve fiber layer defect in the right eye

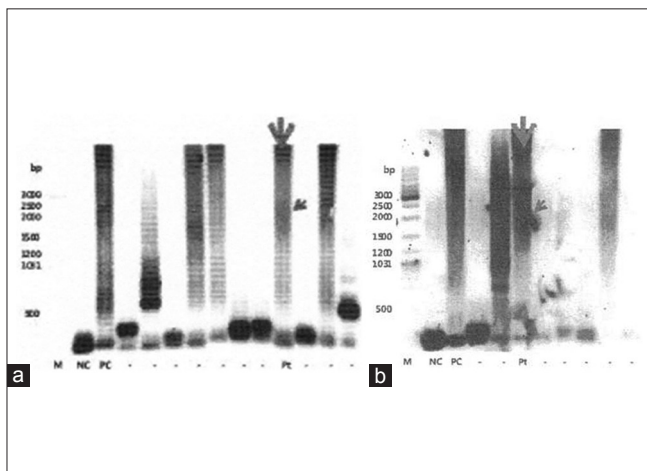


Figure 5: (a) The patient's Southern blot polymerase chain reaction finding consistent with myotonic dystrophy Type 1. Note the unstable expansion of 550 cytosine-thymine-guanine repeats of the dystrophin myotonic-protein kinase gene. (b) The daughter's Southern blot polymerase chain reaction finding. The same finding as her mother was noted

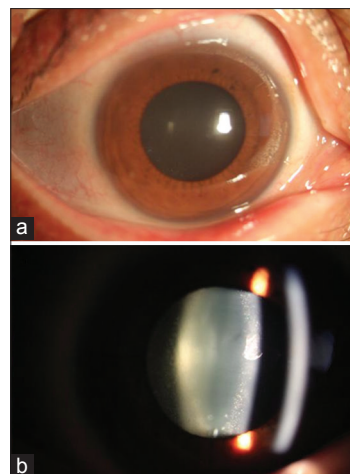


Figure 2: (a) Sluggish pupillary response to mydriatics. (b) Characteristic snowflake cataract

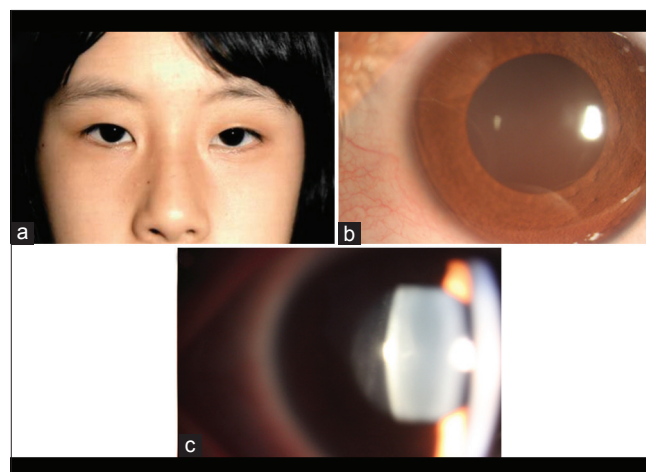


Figure 4: (a) Bilateral ptosis. (b) Sluggish pupillary response to mydriatics. (c) Characteristic snowflake cataract

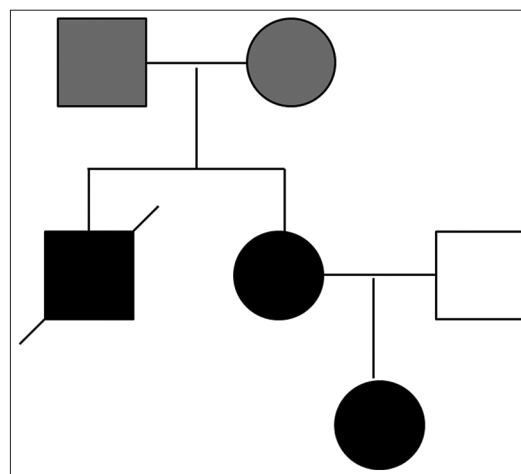


Figure 6: Pedigree of the myotonic dystrophy family. Circle, female; square, male; filled symbol, symptomatic; open symbol, asymptomatic; shaded symbol, affected status not known

heart conduction abnormalities, insulin resistance, premature balding, and cataracts.^[5]

Myotonic dystrophy is inherited in an autosomal dominant fashion via unstable expansions of specific nucleotide sequences, the number of which influences clinical features. DM is classified as two clinical disorders, such as Type 1 and Type 2, caused by an unstable expansion of the CTG trinucleotide repeat in the DMPK gene, or a similar expansion of the cytosine-CTG repeat in intron 1 of the cellular nucleic acid binding protein gene. Patients with larger expansions generally have more severe symptoms.

Ocular symptoms are more severe in DM1 and include ptosis, external ophthalmoplegia, epiphora, pupillary light-near dissociation, early-onset cataract, pigmentary degenerative retinopathy, bilateral optic nerve atrophy, and hypotony.^[6,7] Nearly, all DM1 patients have bilateral iridescent cortical and subcapsular cataracts before the age of 50 years.^[4] In early phases, fine iridescent opacities develop in the cortex, which grow into a stellate cataract in the posterior subcapsular region. When more advanced, these are difficult to differentiate from other cortical cataracts.^[8] Ocular muscles degenerate just as other skeletal muscles, resulting in external ophthalmoplegia, motility disorder, weakness of orbicularis oculi and levator muscle, and ptosis. Retinal pigment epithelium changes can occur, including peripheral retinal degeneration, and result in decreased visual acuity.^[9] Hypotony could be related to increased outflow or decreased aqueous secretion although the pathogenic mechanism remains unclear.^[10]

Our cases presented with cataracts, ptosis, weak pupillary response to mydriatics, low intraocular pressure, increased CDRs, and retinal nerve fiber layer defects. Glaucoma has not previously been associated with myotonic dystrophy, and if it is related to this disorder, the exact pathophysiology should be studied in greater depth.

Because the first patient we examined had ocular complications indicative of myotonic dystrophy, we recommended ophthalmic examination of her daughter despite the lack of systemic symptoms, and she also had ptosis and bilateral iridescent cataracts. Genetic examination revealed the expansion of CTG repeats in the DMPK gene corresponding with myotonic dystrophy and both were diagnosed with DM1. Early-onset iridescent cataracts are a characteristic finding in myotonic dystrophy, so this symptom could help in its diagnosis prior to the manifestation of systemic symptoms. Even though there is no definite cure for myotonic dystrophy and management is symptom based, a precise and early diagnosis is necessary for appropriate medical monitoring and

management of symptoms. This could slow disease progression and lower the mortality, therefore improving the quality of life. In this case, myotonic dystrophy was diagnosed earlier through clinical symptoms with the assistance of genetic evaluation, suggesting that ophthalmic evaluation could help in diagnosing systemic diseases.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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